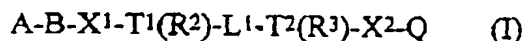


Claims

1. A compound of formula (I)

5



wherein:

A is 5- or 6-membered monocyclic aromatic ring containing 1, 2 or 3 ring heteroatoms

10 selected from nitrogen, oxygen and sulphur atoms optionally substituted by one, two or three atoms or groups selected from halo, oxo, carboxy, trifluoromethyl, cyano, amino, hydroxy, nitro, C₁₋₄alkyl (for example methyl or ethyl), C₁₋₄alkoxy (for example methoxy or ethoxy), C₁₋₄alkoxycarbonyl, C₁₋₄alkylamino (for example methylamino or ethylamino) or di-C₁₋₄alkylamino (for example dimethylamino or diethylamino);

15

B is a phenylene ring optionally substituted by one or two substituents selected from halo, trifluoromethyl, trifluoromethoxy, cyano, nitro, C₁₋₄alkyl, C₂₋₄alkenyl and C₂₋₄alkynyl, from the substituent -(CH₂)_nY¹ wherein n is 0-4 and Y¹ is selected from hydroxy, amino, carboxy, C₁₋₄alkoxy, C₂₋₄alkenyloxy, C₂₋₄alkynyloxy, C₁₋₄alkylamino, di-C₁₋₄alkylamino, pyrrolidin-

20 1-yl, piperidino, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-

dioxothiomorpholino, piperazin-1-yl, 4-C₁₋₄alkylpiperazin-1-yl, C₁₋₄alkylthio, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphonyl, C₂₋₄alkanoylamino, benzamido, C₁₋₄alkylsulphonamido and phenylsulphonamido, from the substituent -(CH₂)_nY² wherein n is 0-4 and Y² is selected from carboxy, carbamoyl, C₁₋₄alkoxycarbonyl, N-C₁₋₄alkylcarbamoyl, N,N-di-C₁₋

25 4alkylcarbamoyl, pyrrolidin-1-ylcarbonyl, piperidinocarbonyl, morpholinocarbonyl, thiomorpholinocarbonyl,

1-oxothiomorpholinocarbonyl, 1,1-dioxothiomorpholinocarbonyl, piperazin-1-ylcarbonyl,

4-C₁₋₄alkylpiperazin-1-ylcarbonyl, C₁₋₄alkylsulphonamidocarbonyl,

phenylsulphonamidocarbonyl and benzylsulphonamidocarbonyl, from a substituent of the

30 formula -X³-L²-Y² wherein X³ is a group of the formula CON(R³), CON(L²-Y²), C(R³)₂O, O, N(R³) or N(L²-Y²), L² is C₁₋₄alkylene, Y² has any of the meanings defined immediately hereinbefore and each R³ is independently hydrogen or C₁₋₄alkyl, and from a substituent of the formula -X³-L³-Y¹ wherein X³ is a group of the formula CON(R³), CON(L³-Y¹), C(R³)₂O,

- O, N(R³) or N(L¹-Y¹), L¹ is C₂₋₄alkylene, Y¹ has any of the meanings defined immediately hereinbefore and each R³ is independently hydrogen or C₁₋₄alkyl, and wherein any heterocyclic group in a substituent of B optionally bears 1 or 2 substituents selected from carboxy, carbamoyl, C₁₋₄alkyl, C₁₋₄alkoxycarbonyl, N-C₁₋₄alkylcarbamoyl and
- 5 N,N-di-C₁₋₄alkylcarbamoyl, and wherein any phenyl group in a substituent of B optionally bears 1 or 2 substituents selected from halo, trifluoromethyl, cyano, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₁₋₄alkoxy, C₂₋₄alkenyloxy and C₂₋₄alkynyloxy; T¹ is CH or N;
- 10 T² is CH or N; with the proviso that at least one of T¹ and T² is N and wherein the heterocyclic ring formed by T¹, T², L¹, R² and R³ is optionally substituted by one or two substituents selected from hydroxy, oxo, carboxy and C₁₋₄alkoxycarbonyl; or one of the following:
- 15 $-(CH_2)_n-R$, $-(CH_2)_n-NRR^1$, $-CO-R$, $-CO-NRR^1$, $-(CH_2)_n-CO-R$ and $-(CH_2)_n-CO-NRR^1$; wherein n is 0, 1 or 2, preferably n is 1 or 2; R and R¹ are independently selected from hydrogen, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, hydroxyC₁₋₄alkyl, carboxyC₁₋₄alkyl and C₁₋₄alkoxycarbonylC₁₋₄alkyl or where possible R
- 20 and R¹ may together form a 5- or 6-membered optionally substituted saturated or partially unsaturated (preferably saturated) heterocyclic ring which may include in addition to the nitrogen to which R and R¹ are attached 1 or 2 additional heteroatoms selected from nitrogen, oxygen and sulphur X¹ is SO, SO₂, C(R⁴)₂ or CO when T¹ is CH or N; or in addition X¹ is O or S when T¹ is CH;
- 25 and wherein each R⁴ is independently hydrogen or C₁₋₄alkyl;
- L¹ is C₁₋₄alkylene or C₁₋₃alkylenecarbonyl;
- ~~R² is hydrogen or C₁₋₄alkyl;~~
- R³ is hydrogen or C₁₋₄alkyl;
- or R² and R³ are joined to form a C₁₋₄alkylene or -CH₂CO- group; wherein the ring formed by
- 30 T¹, R², R³, T² and L¹ is optionally substituted; with the proviso that when T¹ and T² are both N, L¹ is not methylene and R² and R³ together are not methylene;

X^2 is $S(O)_y$, wherein y is one or two, $C(R^3)_2$ or CO ; and each R^3 is hydrogen or C_{1-4} alkyl;

Q is phenyl, naphthyl, phenyl C_{1-4} alkyl, phenyl C_{2-4} alkenyl, phenyl C_{2-4} alkynyl or a heterocyclic moiety containing up to 4 heteroatoms selected from nitrogen, oxygen and sulphur and Q is optionally substituted by one, two or three substituents selected from halo, trifluoromethyl,

5 trifluoromethoxy, cyano, hydroxy, amino, nitro, trifluoromethylsulphonyl, carboxy, carbamoyl, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, C_{2-4} alkenyloxy, C_{2-4} alkynyloxy, C_{1-4} alkylthio, C_{1-4} alkylsulphinyl, C_{1-4} alkylsulphonyl, C_{1-4} alkylamino, di- C_{1-4} alkylamino, C_{1-4} alkoxycarbonyl, N - C_{1-4} alkylcarbamoyl, N,N -di- C_{1-4} alkylcarbamoyl, C_{2-4} alkanoyl, C_{2-4} alkanoylamino, hydroxy C_{1-4} alkyl, C_{1-4} alkoxy C_{1-4} alkyl, carboxy C_{1-4} alkyl, C_{1-4} alkoxycarbonyl C_{1-4} alkyl, carbamoyl C_{1-4} alkyl, N - C_{1-4} alkylcarbamoyl C_{1-4} alkyl, N,N -di- C_{1-4} alkylcarbamoyl C_{1-4} alkyl, phenyl, heteroaryl, phenoxy, phenylthio, phenylsulphinyl, phenylsulphonyl, benzyl, benzoyl, heteroaryloxy, heteroarylthio, heteroarylsulphinyl and heteroarylsulphonyl, and wherein said heteroaryl substituent or the heteroaryl group in a heteroaryl-containing substituent is a 5- or 6-membered monocyclic heteroaryl ring containing

10 up to 3 heteroatoms selected from nitrogen, oxygen and sulphur, and wherein said phenyl, heteroaryl, phenoxy, phenylthio, phenylsulphinyl, phenylsulphonyl, heteroaryloxy, heteroarylthio, heteroarylsulphinyl, heteroarylsulphonyl, benzyl or benzoyl substituent optionally bears 1, 2 or 3 substituents selected from halo, trifluoromethyl, cyano, hydroxy, amino, nitro, carboxy, carbamoyl, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylamino, di- C_{1-4} alkylamino, C_{1-4} alkoxycarbonyl, N - C_{1-4} alkylcarbamoyl, N,N -di- C_{1-4} alkylcarbamoyl and C_{2-4} alkanoylamino; and pharmaceutically acceptable salts thereof.

2. A compound of formula (I) according to claim 1 wherein A is a pyridyl, pyrimidinyl or pyridazinyl ring.

3. A compound of formula (I) according to claim 2 wherein A is 4-pyrimidinyl or 4-pyridyl.

4. A compound of formula (I) according to any one of claims 1 to 3 wherein B is paraphenylene.

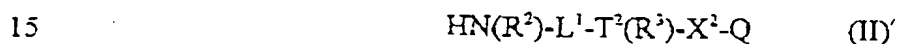
5. A compound of formula (I) according to any one of claims 1 to 4 wherein the ring formed by T¹, R², R³, T² and L is 1,4-piperazinediyl.
- 5 6. A compound of formula (I) according to any one of claims 1 to 5 wherein X¹ is CO.
7. A compound of formula (I) according to any one of claims 1 to 6 wherein X² is SO₂.
8. A compound of formula (I), as defined in claim 1, wherein
- 10 A is pyridyl, pyrimidinyl, or pyridazinyl;
B is para-phenylene;
X¹ is CO, SO₂ or CH₂;
T¹ and T² are both N;
L¹ is ethylene or propylene;
- 15 R² and R³ are joined to form an ethylene or propylene or methylenecarbonyl group;
X² is SO₂;
Q is styryl or naphthyl optionally substituted by fluoro, chloro or bromo or is phenyl optionally substituted by fluorophenyl, chlorophenyl, or bromophenyl;
and pharmaceutically-acceptable salts thereof.
- 20 9. A compound of formula (I) selected from:
1-(6-bromonaphth-2-ylsulphonyl)-4-[4-(4-pyrimidinyl)benzoyl]piperazine;
1-(6-chloronaphth-2-ylsulphonyl)-4-[4-(4-pyridyl)benzoyl]piperazine;
1-(6-bromonaphth-2-ylsulphonyl)-4-[4-(4-pyridazinyl)benzoyl]piperazine;
- 25 and pharmaceutically-acceptable salts thereof.
-
- ~~10. A compound of formula (I) according to any one of claims 1 to 9 for use in medical therapy.~~
- 30 11. A pharmaceutical formulation comprising a compound of formula (I) according to any one of claims 1 to 9 and a pharmaceutically-acceptable diluent or carrier.

12. Use of a compound of formula (I) according to any one of claims 1 to 9 in the preparation of a medicament for use in producing a Factor Xa inhibiting effect.

13. A method of preventing or treating a Factor Xa mediated disease or medical condition comprising administering to a patient a pharmaceutically effective amount of a compound of formula (I), as defined in any one of claims 1 to 9.

14. A process for preparing a compound of formula (I), are defined in claim 1,
comprising:

(a) for the production of those compounds of the formula (I) wherein T¹ is N and X¹ is CO, the reaction, conveniently in the presence of a suitable base, of an amine of formula (II)

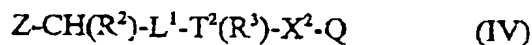


with an acid of the formula (III)



or a reactive derivative thereof;

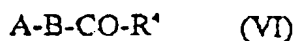
(b) for the production of those compounds of the formula (I) wherein T¹ is CH and X¹ is O by the reaction, conveniently in the presence of a suitable coupling agent, of a compound of the formula (IV):



wherein Z is a displaceable group, with a phenolic compound of the formula (V):



(c) for the production of those compounds of the formula (I) wherein T¹ is N and X¹ is CH(R⁴), the reductive amination of a keto compound of the formula (VI):

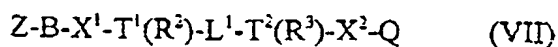


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wherein R⁴ is hydrogen or C₁₋₄ alkyl, with an amine of the formula (II) as defined above;

(d) the reaction of a compound of the formula (VII):

10



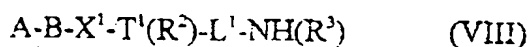
wherein Z is a displaceable group with an activated derivative of ring A;

(e) by forming A ring on compounds of formula (VII), wherein Z is a functional group capable of cyclisation;

15

(f) for the production of compounds wherein T² is N, the reaction of a compound of the formula (VIII):

20



with a compound of the formula (IX):

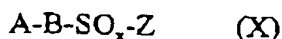


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wherein Z is a displaceable group;

(g) for the production of compounds wherein T¹ is N and X¹ is SO or SO₂, the reaction of a compound of the formula (II) as defined above with a compound of the formula (X):

30



wherein x is one or two and Z is a displaceable group;

(h) for production of compounds of formula (I) by coupling T² to Q and thus preparing
5 the -T²-X²-Q moiety, methods analogous to those described in process variants (a), (c) and (g)
for preparing the B-X¹-T¹- moiety may be employed;

(i) for the production of compounds of formula (I) wherein X¹ is a group of the
formula SO, SO₂, wherein B bears a C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl,
10 1-oxothiomorpholino or 1,1-dioxothiomorpholino group, wherein X² is a group of the formula
SO or SO₂ wherein Q bears a C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl, phenylsulphinyl,
phenylsulphonyl, heteroarylsulphinyl or heteroarylsulphonyl group, the oxidation of the
corresponding compound of the formula (I) which contains X¹ as a thio group.